



The Dietary Pattern Concerning Non-alcoholic Fatty Liver: An Umbrella Review and Meta-analyses of Observational Studies and Intervention Trials

Shima Moradi ^{1,*}, Beitollah Alipour², Mehdi Moradinazar³, Azadeh Heydarian⁴, Sahar Cheshmeh⁵, Fatemeh Sadeghi¹, Yahya Pasdar²

¹ Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

² Department of Nutrition Sciences, School of Nutritional Sciences and Food Technology, Kermanshah University of Medical Sciences, Kermanshah, Iran

³ Clinical Research Development Center, Imam Khomeini and Mohammad Kermanshahi and Farabi Hospitals, Kermanshah University of Medical Sciences, Kermanshah, Iran

⁴ Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Tehran, Iran

⁵ Department of Molecular and Experimental Nutritional Medicine, University of Potsdam, Nuthetal, Germany

*Corresponding author: Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran. Email: shima.moradi400@yahoo.com

Received 2023 November 5; Accepted 2024 May 21.

Abstract

Context: Non-alcoholic fatty liver disease (NAFLD) has been extensively studied in recent years, but the optimal dietary patterns for improving this condition remain unclear.

Evidence Acquisition: Therefore, this umbrella review aimed to summarize the available evidence from meta-analyses on the relationship between various dietary patterns and NAFLD.

Results: Two independent researchers identified published meta-analyses of interventional and observational studies that investigated the relationship between dietary patterns and NAFLD by searching electronic databases up until March 2023 and extracting relevant information. The pooled effect size of dietary patterns on NAFLD was evaluated using the standard mean difference (SMD) with a 95% confidence interval (CI). Fourteen meta-analyses met the inclusion criteria.

Conclusions: All NAFLD-related outcomes, including hepatic steatosis, Fatty Liver Index (FLI), liver stiffness, and liver enzymes, were significantly affected by a calorie-restricted diet. Similarly, following the Mediterranean diet had beneficial effects on improving these outcomes. The findings support the role of a calorie-restricted diet and a Mediterranean diet in improving NAFLD, alongside the treatment protocol for these patients.

Keywords: Dietary Pattern, Non-alcoholic Fatty Liver Disease, Calorie-Restricted Diet, Mediterranean Diet

1. Context

Non-alcoholic fatty liver disease (NAFLD) is one of the leading causes of chronic liver disorders (1, 2). It is estimated that 25% of the global population suffers from NAFLD (3), which is characterized by the accumulation of triglycerides in liver hepatocytes (4). Conditions such as obesity, metabolic syndrome, and type 2 diabetes can contribute to its development (5). The consequences of NAFLD range from non-alcoholic steatohepatitis (NASH) to fibrosis, cirrhosis, hepatocellular carcinoma, and eventually death (3, 6). A recent meta-analysis reported that patients with NAFLD have an increased risk of

cardiovascular disease, stroke, breast cancer, and colorectal cancer (7).

Diet, in addition to contributing to the development of NAFLD, can also play a role in its treatment. Therefore, weight loss or maintaining a healthy weight can reduce inflammation and improve fatty liver (8, 9). Healthy dietary patterns, which include plenty of fruits, vegetables, and whole grains while limiting saturated fatty acids, trans fats, and simple sugars, have been suggested to help prevent and manage chronic diseases (10). Studies have shown that an increased intake of energy-dense foods, such as those high in saturated fats and simple sugars, is associated with the development

of fatty liver disease (9). Evidence from observational studies suggests that a Western diet is linked to the occurrence of NAFLD, while adherence to a healthy dietary pattern is associated with a reduced risk of developing the disease (11).

Meta-analyses and systematic reviews have examined the effects of dietary patterns such as low-carbohydrate diets, Mediterranean diets, and calorie-restricted diets on the progression of NAFLD. Given the increasing prevalence of NAFLD and research in this area, an umbrella review of systematic reviews and meta-analyses is warranted to determine the most effective dietary approach for improving, preventing, and reducing the incidence of NAFLD.

2. Evidence Acquisition

This umbrella review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (12).

2.1. Protocol and Registration

The protocol for this umbrella review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42022377459).

2.2. Search Strategy, Inclusion, and Exclusion Criteria

The research question and the inclusion and exclusion criteria were developed using the Population, Interventions, Comparators, Outcomes, and Study Design (PICOS) framework (Appendix 1 in Supplementary File). Two independent researchers conducted a systematic search of electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, up to March 3, 2023. Both Medical Subject Headings (MeSH) and non-MeSH keywords were used (Appendix 2 in Supplementary File), and references from relevant articles were reviewed to avoid missing any pertinent studies. No restrictions were imposed based on language, time, or location in the systematic search.

Eligible studies for inclusion were systematic reviews and meta-analyses that met the following criteria: (1) calculated random-effects sizes with a 95% confidence interval (CI); (2) conducted on adults; and (3) included dietary patterns as the exposure. Non-alcoholic fatty liver disease was considered the outcome of interest. The initial search yielded 333 articles, of which 68 were duplicates. After removing these duplicates, 265 articles remained. Of these, 58 were excluded because they were irrelevant study types (observational, clinical trials, reviews, etc.), 25 were experimental studies, six were

books, and 11 were unrelated. A total of 165 articles were assessed in more detail, and 151 additional studies were excluded for the following reasons: Ninety-nine did not examine dietary patterns as the exposure, and 52 did not consider NAFLD as an outcome. After further screening, 19 studies remained, but five were excluded because they did not examine dietary patterns. Ultimately, 14 studies were eligible for inclusion in this review (Figure 1).

2.3. Data Extraction

Data from the eligible studies were independently extracted by two researchers using a standardized data collection checklist. This checklist, formatted as an Excel file, included the following information: Author names, year of publication, country of study, number of included studies, type of studies, sample size, age of participants, type of diet, random-effects size (CI 95%), I^2 statistic, and Egger test P-values. Additionally, data related to NAFLD outcomes, including hepatic steatosis, intrahepatic fat (IHF), Fatty Liver Index (FLI), and related biochemical measures [alanine transaminase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT)], were extracted. Any disagreements were resolved through discussion after completing the forms.

2.4. Quality Assessment

Two researchers independently evaluated the quality of the included studies. In cases of disagreement, a third researcher re-evaluated the studies. The quality assessment was conducted using a measurement tool to assess systematic reviews 2 (AMSTAR-2). A measurement tool to assess systematic reviews 2 assesses the quality of studies by asking the following 16 questions: (1) PICOS components; (2) review protocol; (3) study designs; (4) comprehensive literature search strategy; (5) study selection in duplicate; (6) data extraction in duplicate; (7) list of excluded studies and justification for exclusions; (8) study characteristics; (9) satisfactory techniques for assessing risk of bias; (10) source of funding; (11) appropriate statistical methods; (12) assessing the potential impact of bias on results; (13) accounting for bias when interpreting and discussing results; (14) a satisfactory explanation for and discussion of any heterogeneity; (15) publication bias and related discussion; and (16) conflict of interest.

Each item was rated as "Yes" when fully addressed, "Partial Yes" when it was only partially described, "No" when it was not done, and "Unclear" when it was

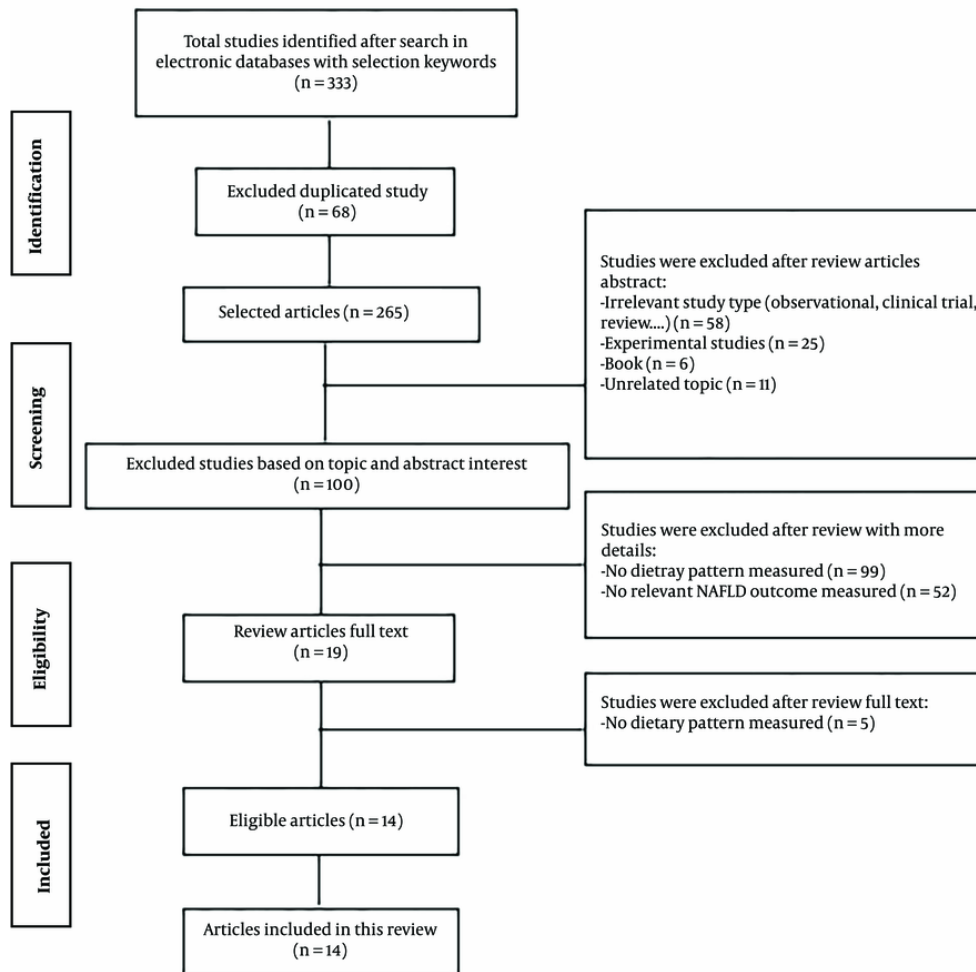


Figure 1. Flowchart of study selection

uncertain if it had been completed (Appendix 3 in Supplementary File).

3. Data Synthesis

The pooled effect sizes from meta-analyses of randomized controlled trials (RCTs) for each outcome before and after dietary interventions were converted into standardized mean differences (SMDs) with 95% CI (Tables 1 and 2). Forest plots were created for each outcome based on the dietary pattern type and their effects on NAFLD-related outcomes. All statistical analyses were performed using Stata software version 11.2 (StataCorp, College Station, TX).

4. Results

4.1. Characteristics of Included Systematic Reviews and Meta-analyses

All 14 included studies were conducted between 2016 and 2023, with four conducted in Iran (13, 20, 24, 25), two in Brazil (14, 18), and the others in Cleveland (26), South Korea (17), the UK (15), the USA (19), Finland (21), Japan (16), China (22), and Greece (23). Eleven studies performed meta-analyses exclusively on RCTs (14-24), while two only analyzed observational studies (case-control, cross-sectional, and cohort) (25, 26). Akhlaghi et al. (13) meta-analyzed both observational and

Table 1. Characterization, Data Synthesis, and Bias Assessment of Illegible Studies on Evaluations Related to Non-alcoholic Fatty Liver Disease, Including Hepatic Steatosis, Intrahepatic Fat, and Fatty Liver Index

Author, Year, Reference	Country	Total Number of Study	RCT	Sample Size	Age (y)	Kind of Diet	SMD (CI 95%)	I ² (%)	Egger Test P-Value
Hepatic steatosis									
Akhlaghi et al., 2020, (13)	Iran	13	4	272	-	Mediterranean diet	-1.43 (-3.4, 0.58)	68.9	No publication bias
Garcez et al., 2021, (14)	Brazil	6	2	127	18 - 81	low-carbohydrate diet	0.39 (-1.6, 2.37)	87.56	NR
Haigh et al., 2022, (15)	UK	26	4	233	48.3 ± 5.9	Mediterranean diet	-0.4 (-0.66, 1.61)	76	No publication bias
			4	257	48.3 ± 5.9	calorie-restricted	-5.65 (-7.46, -3.54)	0	No publication bias
FLI									
Haigh et al., 2022, (15)	UK	26	4	228	48.3 ± 5.9	Mediterranean diet	-4.86 (-6.86, -2.86)	71	No publication bias
			1	260	48.3 ± 5.9	Calorie-restricted	-2.54 (-4.54, -0.54)	NR	No publication bias
Kawaguchi et al., 2021, (16)	Japan	6	3	140	33 - 56	Mediterranean diet	-1.06 (-1.95, -0.17)	76	Significant bias for FLI
IHF									
Ahn et al., 2018, (17)	South Korea	11	4	22	NR	Low-carbohydrate diet	1.7 (-0.3, 3.68)	91	NR
Bueno et al., 2019, (18)	Brazil	4	4	183	> 18	Low-carbohydrate diet	-2.64 (-4.64, -0.64)	68.30	NR
Henschel, 2021, (19)	USA	11	4	22	NR	Low-carbohydrate diet	2.38 (0.38, 4.36)	NR	NR
Haghighatdoost et al., 2016, (20)	Iran	10	4	50	> 18	Low-carbohydrate diet	-3.51 (-5.5, -1.51)	83.20	0.34
Houttu et al., 2021, (21)	Finland	8	2	72	38 - 55	Mediterranean diet	-0.57 (-1.04, -0.1)	0	Did not conducted
Liver stiffness									
Haigh et al., 2022, (15)	UK	26	5	271	48.3 ± 5.9	Mediterranean diet	-1.99 (-3.97, 0)	87	No publication bias
			2	193	48.3 ± 5.9	Calorie-restricted	-2.64 (-4.6, -0.67)	0	No publication bias
Yin et al., 2021, (22)	China	6	2	343	≥ 18	Intermittent fasting	0.12 (-1.85, 2.1)	0	Visual inspection of funnel plots
Kawaguchi et al., 2021, (16)	Japan	6	2	72	33 - 56	Mediterranean diet	-0.67 (-1.7, 0.36)	75	No publication bias

Abbreviations: NR, not reported; FLI, Fatty Liver Index; RCT, randomized controlled trials; SMD, standard mean difference; IHF, intrahepatic fat.

interventional studies. Meta-analyses of RCTs had sample sizes ranging from 22 to 667, while observational studies included 301 to 16,823 participants. Bueno et al.'s (18) and Henschel et al.'s (19) studies were letters addressing the study by Ahn et al. (17), who had analyzed the data differently. Consequently, Ahn et al.'s study was excluded in favor of the findings from the other studies (17).

Three of the included studies assessed hepatic steatosis (13-15), two assessed the FLI (15, 16), and five evaluated IHF (17-21) as primary outcomes. Regarding biochemical factors related to liver function, ten studies evaluated ALT (14-17, 19-24), nine assessed AST (14, 15, 17, 19-24), and three measured GGT (20, 21, 24). The examined dietary patterns included the Mediterranean diet, low-carbohydrate diet, moderate-carbohydrate diet, calorie-restricted, hypocaloric diet, intermittent

fasting, gluten-free diet, prudent diet, and Western diet (Tables 1 - 3).

4.2. Hepatic Steatosis

Three meta-analyses (13-15) investigated the effects of the Mediterranean, calorie-restricted, and low-carbohydrate diets on hepatic steatosis (Table 1). As shown in the forest plot (Appendix 4A in Supplementary File), the most significant effect on hepatic steatosis was related to the calorie-restricted diet (SMD: -5.65; CI 95%: -7.46, -3.54), with an I² of 0.

4.3. Fatty Liver Index

This index was evaluated in meta-analyses by Haigh et al. (15) and Kawaguchi et al. (16), both of which showed that the Mediterranean diet significantly

Table 2. Characterization, data synthesis, and bias assessment of illegible studies on Evaluations Related to Non-alcoholic Fatty Liver Disease, Including Biochemical Assessment

Author, Year, Reference	Country	Total Number of Study	RCT	Sample Size	Age (y)	Kind of Diet	SMD (CI 95%)	I ² (%)	Egger Test P-Value
ALT									
Ahn et al., 2018, (17)	South Korea	11	5	33	NR	Low-carbohydrate diet	1.57 (-0.4, 3.56)	73	NR
Henschel et al., 2021, (19)	USA	11	5	33	NR	Low-carbohydrate diet	1.69 (-0.3, 3.69)	NR	NR
Katsagoni et al., 2017, (23)	Greece	20	3		>18	Moderate-carbohydrate diet	0.05 (-0.27, 0.36)	0	No publication bias
Garcez et al., 2021, (6)	Brazil	6	4	204	18 - 81	Low-carbohydrate diet	-0.02 (-2.01, 1.96)	0	NR
Haghighatdoost et al., 2016, (20)	Iran	10	11	230	>18	Low-carbohydrate diet	-1.02 (-3.01, 0.98)	87.90	0.52
Houttu et al., 2021, (21)	Finland	8	2	113	38 - 55	Hypo-caloric diet	-1.09 (-1.49, 0.69)	0	Did not conducted
			2	72	38 - 55	Mediterranean diet	0.07 (-0.39, 0.53)	0	Did not conducted
Haigh et al., 2022, (15)	UK	26	9	413	48.3 ± 5.9	Mediterranean diet	-2.38 (-4.38, -0.38)	81	No publication bias
			8	667	48.3 ± 5.9	Calorie-restricted	-4.24 (-6.25, -2.25)	0	No publication bias
Sangouni et al., 2021, (24)	Iran	10	8	498	≥18	Mediterranean diet	-1.61 (-3.57, 0.39)	NR	0.95
Yin et al., 2021, (22)	China	6	2	194	≥18	Intermittent fasting	-6.08 (-8.09, -4.09)	0	Visual inspection of funnel plots
Kawaguchi et al., 2021, (16)	Japan	6	6	295	33-56	Mediterranean diet	-0.79 (-2.21, 0.62)	96	No publication bias
AST									
Ahn et al., 2018, (17)	South Korea	11	4	54	NR	Low-carbohydrate diet	1.47 (-0.43, 3.52)	77	NR
Henschel et al., 2021, (19)	USA	11	4	54	NR	Low-carbohydrate diet	1.65 (-0.35, 3.65)	NR	NR
Katsagoni et al., 2017, (23)	Greece	20	4		>18	Moderate-carbohydrate diet	0.28 (-0.26, 0.82)	55.60	No publication bias
Garcez et al., 2021, (14)	Brazil	6	5	130	18 - 81	Low-carbohydrate diet	-0.81 (-2.81, 1.19)	0	NR
Haghighatdoost et al., 2016, (20)	Iran	10	10	216	>18	Low-carbohydrate diet	-0.81 (-2.81, 1.19)	61.40	0.38
Houttu et al., 2021, (21)	Finland	8	2	113	38 - 55	Hypo-caloric diet	-0.75 (-1.23, 0.23)	45	Did not conducted
Haigh et al., 2022, (15)	UK	26	6	314	48.3 ± 5.9	Mediterranean diet	-1.8 (-3.8, 0.2)	81	No publication bias
			7	628	48.3 ± 5.9	Calorie-restricted	-1.46 (-3.44, 0.54)	53	No publication bias
Sangouni et al., 2021, (24)	Iran	10	4	197	≥18	Mediterranean diet	-2.2 (-4.09, -0.2)	NR	0.3
Yin et al., 2021, (22)	China	6	2	194	≥18	Intermittent fasting	-7.57 (-9.53, -5.55)	0	Visual inspection of funnel plots
GGT									
Haghighatdoost et al., 2016, (20)	Iran	10	6	92	>18	low-carbohydrate diet	-0.72 (-2.72, 1.28)	99.40	0.86
Houttu et al., 2021, (21)	Finland	8	3	154	38-55	Mediterranean diet	0.04 (-0.28, 0.35)	0	Did not conducted
Sangouni et al., 2021, (24)	Iran	10	9	513	≥18	Mediterranean diet	-2.08 (-4.08, -0.08)	NR	0.44

Abbreviations: NR, not reported; ALT, alanine transaminase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; RCT, randomized controlled trials; SMD, standard mean difference.

reduced the FLI (Table 1 and Appendix 4B in Supplementary File).

4.4. Intrahepatic Fat

The findings indicated that the low-carbohydrate diet improved IHF more effectively than the Mediterranean diet (Appendix 4C in Supplementary File). Ahn et al. initially reviewed the low-carbohydrate diet and did not

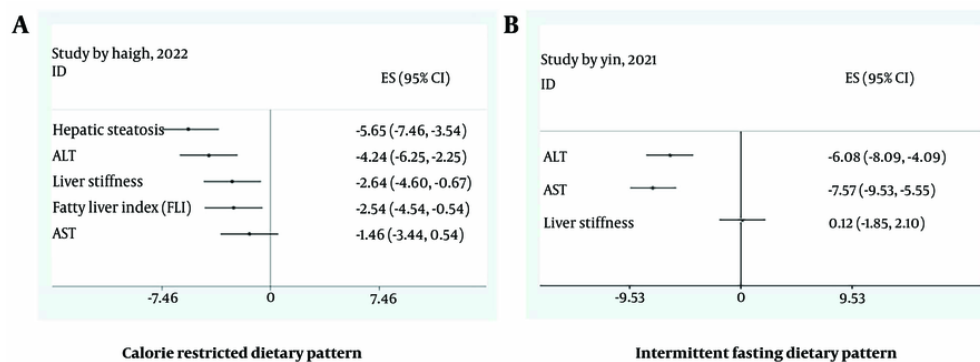
observe a significant effect (17). However, in 2019, Bueno et al. (18) published a letter modifying Ahn's analysis, which revealed a significant effect. Henschel et al. supported these findings in another letter, and Bueno's study was ultimately included in the analyses (19) (Table 1).

4.5. Liver Stiffness

Table 3. Characterization, Data Synthesis, and Bias Assessment of Illegible Studies on the Prevalence of Non-alcoholic Fatty Liver Disease

Author, Year, Reference	Country	Observational Study (N)	Sample Size	Age (y)	Kind of diet	OR (CI 95%)	P Random	I ²	Egger Test P-Value
Aggarwal et al., 2021, (26)	Cleveland	5	301	> 15	Gluten-free diet	0.214 (0.096, 0.413)	< 0.01	97%	NR
Akhlaghi et al., 2019, (13)	Iran	7	16823	NR	Mediterranean diet	0.95 (0.9 - 1)	0.05	68.1%	0.002
Hassani Zadeh et al., 2020, (25)	Iran	5	3057	NR	Mediterranean diet	0.772 (0.602, 0.989)	0.041	NR	0.04
		14	13023	NR	Prudent diet	0.786 (0.719, 0.859)	< 0.001	12.41%	0.15
		10	8787	NR	Western dietary	1.567 (1.277, 1.922)	< 0.001	46.96%	0.01

Abbreviation: NR, not reported.

**Figure 2.** Forest plot for calorie-restricted dietary pattern, A; and intermittent fasting dietary pattern, B about outcome related to NAFLD

Among the studied diets, the calorie-restricted diet had the most significant effect on improving liver stiffness (SMD: -2.64; CI 95%: -4.6, -0.67), with an I² of 0 (15) (Table 1 and Appendix 4D in Supplementary File).

4.6. Biochemical Indicators Related to Liver Function

Ten studies assessed the effects of dietary patterns (low-carbohydrate, moderate-carbohydrate, hypocaloric, calorie-restricted, intermittent fasting, and Mediterranean diet) on serum ALT levels in patients with NAFLD (Table 2). The forest plot (Appendix 5 in Supplementary File) illustrates the effects of these dietary patterns on ALT. Both calorie-restricted (SMD: -4.24; CI 95%: -6.25, -2.25) and intermittent fasting (SMD: 6.08; CI 95%: -8.09, -4.09) diets showed the most significant improvements in ALT levels.

Nine studies evaluated serum AST levels in NAFLD patients. The forest plot (Appendix 6 in Supplementary File) showed that the intermittent fasting diet (SMD:

-7.57; CI 95%: -9.53, -5.55) significantly improved AST levels.

Only three studies, including Sangouni et al. (24), assessed serum GGT levels in NAFLD patients. In 2021, a meta-analysis of nine RCTs demonstrated that the Mediterranean diet significantly improved GGT levels (SMD: -2.08; CI 95%: -4.08, -0.08) (Table 2 Appendix 7 in Supplementary File).

4.7. Calorie-Restricted Diet

The effects of a calorie-restricted diet were evaluated across several liver parameters, including hepatic steatosis, FLI, liver stiffness, ALT, and AST (Figure 2A). As shown in Forest Plot 2, the most significant effect was on hepatic steatosis (SMD: -5.65; CI 95%: -7.46, -3.54).

4.8. Intermittent Fasting Diet

In a meta-analysis by Yin et al. (22), intermittent fasting (including alternate-day fasting and other forms

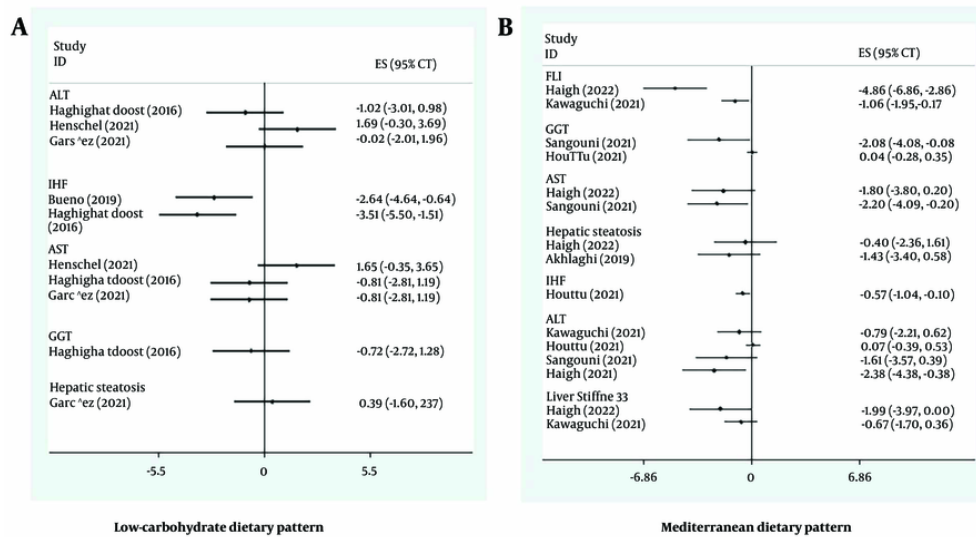


Figure 3. Forest plot for low-carbohydrate dietary pattern, A; and Mediterranean dietary pattern B, about outcome related to Non-alcoholic fatty liver disease (NAFLD)

of periodic caloric restriction) was assessed for its effects on ALT, AST, and liver stiffness. Figure 2B shows that this dietary pattern significantly improved liver enzymes but had no significant effect on liver stiffness.

4.9. Low-carbohydrate Diet

Five meta-analyses investigated the effects of a low-carbohydrate diet on NAFLD-related outcomes. This diet typically reduced carbohydrate intake to 40-50% of daily energy. As shown in Figure 3A, the low-carbohydrate diet was significantly associated with reducing IHF. Studies by Bueno et al. (18) and Haghighatdoost et al. (20) supported these findings. In 2016, Haghighatdoost et al. (20) found that a low-carbohydrate diet (with less than 50% of daily energy from carbohydrates) improved IHF (SMD: -3.51; CI 95%: -5.5, -1.51). A meta-analysis by Bueno et al. (18) showed that a low-carbohydrate diet (40% of daily energy from carbohydrates) significantly reduced IHF (SMD: -2.64; CI 95%: -4.64, -0.64).

4.10. Mediterranean Diet

As depicted in Figure 3B, the Mediterranean diet significantly improved all investigated outcomes, except hepatic steatosis, where the effect was not statistically significant. However, the Mediterranean diet still showed a trend toward reducing hepatic steatosis.

5. Discussion

The findings provided an overview of the best dietary approaches to prevent NAFLD. Among the evaluated dietary patterns, the calorie-restricted diet emerged as the most effective, significantly improving all NAFLD-related outcomes. Similarly, adherence to the Mediterranean diet showed beneficial effects in improving these outcomes. Non-alcoholic fatty liver disease is currently the most common cause of chronic liver disease, and its prevalence is rising (27). At present, there are no successful pharmaceutical treatments for this condition, and several dietary interventions have been suggested (28).

The calorie-restricted diet was shown to improve hepatic steatosis, the FLI, liver stiffness, and liver enzyme levels. This dietary pattern was evaluated in a meta-analysis by Haigh et al. (15) on nine RCTs, which recommended its inclusion in the treatment strategy for NAFLD patients. Historical evidence suggests that reduced dietary intake has been associated with increased life expectancy and reduced non-communicable diseases since the early 19th century. As a result, "calorie restriction" was formally introduced in the late 1930s (29). One mechanism proposed in Asghari et al.'s study (30) suggests that a calorie-restricted diet improves sensitivity to fibroblast growth factor 21 (FGF-21), which is resistant in NAFLD patients. Caloric restriction helps regulate energy homeostasis, fat and

glucose metabolism, and improves inflammatory conditions and oxidative stress-induced damage. Additionally, the beneficial effects of caloric restriction are linked to the induction of the sirtuin family, particularly SIRT1, which protects NAD⁺-dependent enzymes and increases organism lifespan (31). SIRT4 also plays a critical role in fatty acid oxidation in liver cell mitochondria through SIRT1 (32, 33). Moreover, caloric restriction has been shown to reduce proteins associated with liver inflammation in animal models and has beneficial effects on insulin resistance, liver steatosis, lipogenesis enzymes, mitochondrial biogenesis, collagen deposition, and endoplasmic reticulum stress (33). Therefore, the findings of this study support the use of calorie restriction in conjunction with other treatment approaches for NAFLD patients.

The present umbrella review also highlighted the Mediterranean diet's role in improving NAFLD-related outcomes. The Mediterranean diet is characterized by high consumption of plant-based foods, including fruits, vegetables, legumes, nuts, and whole grains. Olive oil is the primary source of dietary fat, and moderate consumption of red wine, fresh fish, dairy products, poultry, and eggs is recommended, while red and processed meats are limited (34). Nutritionally, this diet is rich in monounsaturated and polyunsaturated fatty acids (PUFAs) and fiber, while refined grains and foods with added sugars are limited (35). These components reduce inflammation and oxidative stress, offering preventive effects against NAFLD. The Mediterranean diet also includes PUFAs, particularly omega-3 fatty acids, and a lower ratio of omega-6 to omega-3 fatty acids, which help prevent liver fat accumulation and reduce hepatic steatosis (36, 37).

An essential component of the Mediterranean diet is olive oil, which has demonstrated anti-inflammatory and antioxidant properties in improving NAFLD (35, 38). Another crucial aspect is the high fiber content from whole grains and complex carbohydrates, which have a Low Glycemic Index and are low in fructose and added sugars (39, 40). The diet's fiber content helps promote the growth of bacteria that produce short-chain fatty acids with anti-inflammatory properties, thereby reducing fat accumulation in the liver through their metabolism (41, 42). Furthermore, since fructose accelerates fat accumulation in the liver by increasing lipogenesis and fat oxidation, reducing added sugar intake—especially fructose—may significantly lower liver fat accumulation (43, 44). The Mediterranean diet also restricts saturated fat intake by limiting red and processed meats, further reducing liver fat

accumulation, while balanced consumption of poultry and fish provides healthier alternatives (45). Overall, the Mediterranean diet represents a healthy dietary pattern that contrasts with the “Western diet,” which has been reported to increase the risk of NAFLD in Hassani Zadeh's meta-analysis (25).

This umbrella review had several limitations. First, although the systematic search was conducted without restrictions, the potential for missed unpublished reports and archived records cannot be ruled out. Additionally, the number of meta-analyses on prospective studies was limited, and the long-term effects of dietary patterns could not be fully assessed. Therefore, future meta-analyses should focus on more prospective studies to better understand the long-term effects of specific dietary patterns on NAFLD.

5.1. Conclusions

The findings of this umbrella review summarize, for the first time, meta-analyses on dietary patterns and NAFLD. The calorie-restricted diet demonstrated the most significant improvements in NAFLD-related outcomes. Based on these findings, the Mediterranean diet can also be considered an effective treatment approach for NAFLD patients.

Acknowledgements

The authors would like to thank and acknowledge the Kermanshah University of Medical Science for financial support.

Supplementary Material

Supplementary material(s) is available [here](#) [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

Authors' Contribution: Study conception and design: Shima Moradi, Mehdi Moradinazar, Amir Saber; search and data extraction: Shima Moradi, Azadeh Heydarian, Fatemeh Sadeghi; data analysis and interpretation: Shima Moradi, Mehdi Moradinazar, Yahya Pasdar; drafting of the article: Shima Moradi, Yahya Pasdar; critical revision of the article: Sahar Cheshmeh, Shima Moradi, Yahya Pasdar, Amir Saber. All authors agree with the manuscript and declare that the content has not been published elsewhere, as well as they agree to the

proposal of new authorship shown in this revised manuscript.

Conflict of Interests Statement: On behalf of all co-authors, the corresponding author states that there is no conflict of interest.

Data Availability: The datasets used and analyzed during the current study will be available from the corresponding author upon reasonable request.

Funding/Support: This study has not received any funding.

References

- Dreher ML. Dietary patterns, foods, nutrients and phytochemicals in non-alcoholic fatty liver disease. In: Dreher ML, editor. *Dietary patterns and whole plant foods in aging and disease*. Cham, Switzerland: Humana Press; 2018. p. 291-311.
- Pasdar Y, Moradi S, Moludi J, Darbandi M, Niazi P, Nachvak SM, et al. Risk of metabolic syndrome in non-alcoholic fatty liver disease patients. *Mediterranean J Nutrition Metab*. 2019;**12**(4):353-63. <https://doi.org/10.3233/mnm-190290>.
- Ye Q, Zou B, Yeo YH, Li J, Huang DQ, Wu Y, et al. Global prevalence, incidence, and outcomes of non-obese or lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2020;**5**(8):739-52. [PubMed ID: 32413340]. [https://doi.org/10.1016/S2468-1253\(20\)30077-7](https://doi.org/10.1016/S2468-1253(20)30077-7).
- Diniz TA, de Lima Junior EA, Teixeira AA, Biondo LA, da Rocha LAF, Valadao IC, et al. Aerobic training improves NAFLD markers and insulin resistance through AMPK-PPAR-alpha signaling in obese mice. *Life Sci*. 2021;**266**:118868. [PubMed ID: 33310034]. <https://doi.org/10.1016/j.lfs.2020.118868>.
- Barchetta I, Cimini FA, Cavallo MG. Vitamin D Supplementation and Non-Alcoholic Fatty Liver Disease: Present and Future. *Nutrients*. 2017;**9**(9). [PubMed ID: 28906453]. [PubMed Central ID: PMC5622775]. <https://doi.org/10.3390/nu9091015>.
- Gerges SH, Wahdan SA, Elsherbiny DA, El-Demerdash E. Non-alcoholic fatty liver disease: An overview of risk factors, pathophysiological mechanisms, diagnostic procedures, and therapeutic interventions. *Life Sci*. 2021;**271**:119220. [PubMed ID: 33592199]. <https://doi.org/10.1016/j.lfs.2021.119220>.
- Veracruz N, Hameed B, Saab S, Wong RJ. The Association Between Nonalcoholic Fatty Liver Disease and Risk of Cardiovascular Disease, Stroke, and Extrahepatic Cancers. *J Clin Exp Hepatol*. 2021;**11**(1):45-81. [PubMed ID: 33679048]. [PubMed Central ID: PMC7897860]. <https://doi.org/10.1016/j.jceh.2020.04.018>.
- Hannah WN, Harrison SA. Lifestyle and Dietary Interventions in the Management of Nonalcoholic Fatty Liver Disease. *Dig Dis Sci*. 2016;**61**(5):1365-74. [PubMed ID: 27052013]. <https://doi.org/10.1007/s10620-016-4153-y>.
- Kalafati IP, Borsa D, Dimitriou M, Revenas K, Kokkinos A, Dedoussis GV. Dietary patterns and non-alcoholic fatty liver disease in a Greek case-control study. *Nutrition*. 2019;**61**:105-10. [PubMed ID: 30708259]. <https://doi.org/10.1016/j.nut.2018.10.032>.
- Neuhouser ML. The importance of healthy dietary patterns in chronic disease prevention. *Nutr Res*. 2019;**70**:3-6. [PubMed ID: 30077352]. [PubMed Central ID: PMC6328339]. <https://doi.org/10.1016/j.nutres.2018.06.002>.
- Salehi-Sahlabadi A, Sadat S, Beigrezaei S, Pourmasomi M, Feizi A, Ghiasvand R, et al. Dietary patterns and risk of non-alcoholic fatty liver disease. *BMC Gastroenterol*. 2021;**21**(1):41. [PubMed ID: 33509112]. [PubMed Central ID: PMC7844966]. <https://doi.org/10.1186/s12876-021-01612-z>.
- Moher D, Liberati A, Tetzlaff J, Altman DG; Prisma Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;**6**(7). e1000097. [PubMed ID: 19621072]. [PubMed Central ID: PMC2707599]. <https://doi.org/10.1371/journal.pmed.1000097>.
- Akhlaghi M, Ghasemi-Nasab M, Riasatian M. Mediterranean diet for patients with non-alcoholic fatty liver disease, a systematic review and meta-analysis of observational and clinical investigations. *J Diabetes Metab Disord*. 2020;**19**(1):575-84. [PubMed ID: 32550210]. [PubMed Central ID: PMC7271299]. <https://doi.org/10.1007/s40200-019-00475-2>.
- Garcez LS, Avelar CR, Fonseca NSS, Costa PRF, Lyra AC, Cunha CM, et al. Effect of dietary carbohydrate and lipid modification on clinical and anthropometric parameters in nonalcoholic fatty liver disease: a systematic review and meta-analysis. *Nutr Rev*. 2021;**79**(12):1321-37. [PubMed ID: 33515021]. <https://doi.org/10.1093/nutrit/nuaa146>.
- Haigh L, Kirk C, El Gendy K, Gallacher J, Errington L, Mathers JC, et al. The effectiveness and acceptability of Mediterranean diet and calorie restriction in non-alcoholic fatty liver disease (NAFLD): A systematic review and meta-analysis. *Clin Nutr*. 2022;**41**(9):1913-31. [PubMed ID: 35947894]. <https://doi.org/10.1016/j.clnu.2022.06.037>.
- Kawaguchi T, Charlton M, Kawaguchi A, Yamamura S, Nakano D, Tsutsumi T, et al. Effects of Mediterranean Diet in Patients with Nonalcoholic Fatty Liver Disease: A Systematic Review, Meta-Analysis, and Meta-Regression Analysis of Randomized Controlled Trials. *Semin Liver Dis*. 2021;**41**(3):225-34. [PubMed ID: 34147036]. <https://doi.org/10.1055/s-0041-1723751>.
- Ahn J, Jun DW, Lee HY, Moon JH. Critical appraisal for low-carbohydrate diet in nonalcoholic fatty liver disease: Review and meta-analyses. *Clin Nutr*. 2019;**38**(5):2023-30. [PubMed ID: 30314924]. <https://doi.org/10.1016/j.clnu.2018.09.022>.
- Bueno NB, Dos Santos Silva MM, de Melo ISV. Low-carbohydrate diets and intrahepatic lipid content in individuals with non-alcoholic fatty liver disease: Evidence from a meta-analysis of randomized trials. *Clin Nutr*. 2020;**39**(1):310-1. [PubMed ID: 31791671]. <https://doi.org/10.1016/j.clnu.2019.11.026>.
- Henschel B, Dickinson SL, Allison DB. Errors in meta-analysis should be corrected in "Critical appraisal for low-carbohydrate diet in non-alcoholic fatty liver disease: Review and meta-analyses". *Clinical Nutrition*. 2021;**40**(7):4535-6. <https://doi.org/10.1016/j.clnu.2021.05.022>.
- Haghighatdoost F, Salehi-Abargouei A, Surkan PJ, Azadbakht L. The effects of low carbohydrate diets on liver function tests in nonalcoholic fatty liver disease: A systematic review and meta-analysis of clinical trials. *J Res Med Sci*. 2016;**21**:53. [PubMed ID: 27904598]. [PubMed Central ID: PMC5122212]. <https://doi.org/10.4103/1735-1995.187269>.
- Houttu V, Csader S, Nieuwdorp M, Holleboom AG, Schwab U. Dietary Interventions in Patients With Non-alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis. *Front Nutr*. 2021;**8**:716783. [PubMed ID: 34368214]. [PubMed Central ID: PMC8339374]. <https://doi.org/10.3389/fnut.2021.716783>.
- Yin C, Li Z, Xiang Y, Peng H, Yang P, Yuan S, et al. Effect of Intermittent Fasting on Non-Alcoholic Fatty Liver Disease: Systematic Review and Meta-Analysis. *Front Nutr*. 2021;**8**:709683. [PubMed ID: 34322514]. [PubMed Central ID: PMC8310935]. <https://doi.org/10.3389/fnut.2021.709683>.
- Katsagoni CN, Georgoulis M, Papatheodoridis GV, Panagiotakos DB, Kontogianni MD. Effects of lifestyle interventions on clinical characteristics of patients with non-alcoholic fatty liver disease: A meta-analysis. *Metabolism*. 2017;**68**:119-32. [PubMed ID: 28183444]. <https://doi.org/10.1016/j.metabol.2016.12.006>.

24. Sangouni AA, Hassani Zadeh S, Mozaffari-Khosravi H, Hosseinzadeh M. Effect of Mediterranean diet on liver enzymes: a systematic review and meta-analysis of randomised controlled trials. *Br J Nutr*. 2022;**128**(7):1231-9. [PubMed ID: 34165054]. <https://doi.org/10.1017/S0007114521002270>.
25. Hassani Zadeh S, Mansoori A, Hosseinzadeh M. Relationship between dietary patterns and non-alcoholic fatty liver disease: A systematic review and meta-analysis. *J Gastroenterol Hepatol*. 2021;**36**(6):1470-8. [PubMed ID: 33269500]. <https://doi.org/10.1111/jgh.15363>.
26. Aggarwal M, Kumar P, Garg R, Lindenmeyer CC, Wakim-Fleming J, Rubio-Tapia A. S1337 Increased Rate of Nonalcoholic Fatty Liver Disease After Gluten Free Diet in Celiac Disease: A Systematic Review and Meta-Analysis. *Am J Gastroenterol*. 2021;**116**(1):S616. <https://doi.org/10.14309/01.ajg.0000778880.25109.b2>.
27. Cheng R, Wang L, Le S, Yang Y, Zhao C, Zhang X, et al. A randomized controlled trial for response of microbiome network to exercise and diet intervention in patients with nonalcoholic fatty liver disease. *Nat Commun*. 2022;**13**(1):2555. [PubMed ID: 35538056]. [PubMed Central ID: PMC9091228]. <https://doi.org/10.1038/s41467-022-29968-0>.
28. Fernandez T, Vinuela M, Vidal C, Barrera E. Lifestyle changes in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis. *PLoS One*. 2022;**17**(2). e0263931. [PubMed ID: 35176096]. [PubMed Central ID: PMC8853532]. <https://doi.org/10.1371/journal.pone.0263931>.
29. Hwangbo DS, Lee HY, Abozaid LS, Min KJ. Mechanisms of Lifespan Regulation by Calorie Restriction and Intermittent Fasting in Model Organisms. *Nutrients*. 2020;**12**(4). [PubMed ID: 32344591]. [PubMed Central ID: PMC7230387]. <https://doi.org/10.3390/nu12041194>.
30. Asghari S, Rezaei M, Rafrat M, Taghizadeh M, Asghari-Jafarabadi M, Ebadi M. Effects of Calorie Restricted Diet on Oxidative/Antioxidative Status Biomarkers and Serum Fibroblast Growth Factor 21 Levels in Nonalcoholic Fatty Liver Disease Patients: A Randomized, Controlled Clinical Trial. *Nutrients*. 2022;**14**(12). [PubMed ID: 35745238]. [PubMed Central ID: PMC9231395]. <https://doi.org/10.3390/nu14122509>.
31. Lee SH, Lee JH, Lee HY, Min KJ. Sirtuin signaling in cellular senescence and aging. *BMB Rep*. 2019;**52**(1):24-34. [PubMed ID: 30526767]. [PubMed Central ID: PMC6386230]. <https://doi.org/10.5483/BMBRep.2019.52.1.290>.
32. Tauriainen E, Luostarinen M, Martonen E, Finckenberg P, Kovalainen M, Huotari A, et al. Distinct effects of calorie restriction and resveratrol on diet-induced obesity and Fatty liver formation. *J Nutr Metab*. 2011;**2011**:525094. [PubMed ID: 21977315]. [PubMed Central ID: PMC3184417]. <https://doi.org/10.1155/2011/525094>.
33. Zydorczyk C, Li N, Rigal E, Chehade H, Mosig D, Armengaud JB, et al. Calorie Restriction in Adulthood Reduces Hepatic Disorders Induced by Transient Postnatal Overfeeding in Mice. *Nutrients*. 2019;**11**(11). [PubMed ID: 31744052]. [PubMed Central ID: PMC6893580]. <https://doi.org/10.3390/nu11112796>.
34. Seifu CN, Fahey PP, Hailemariam TG, Frost SA, Atlantis E. Dietary patterns associated with obesity outcomes in adults: an umbrella review of systematic reviews. *Public Health Nutr*. 2021;**24**(18):6390-414. [PubMed ID: 33612135]. [PubMed Central ID: PMC1148623]. <https://doi.org/10.1017/S1368980021000823>.
35. Plaz Torres MC, Aghemo A, Lleo A, Bodini G, Furnari M, Marabotto E, et al. Mediterranean Diet and NAFLD: What We Know and Questions That Still Need to Be Answered. *Nutrients*. 2019;**11**(12). [PubMed ID: 31817398]. [PubMed Central ID: PMC6949938]. <https://doi.org/10.3390/nu11122971>.
36. de Castro GS, Calder PC. Non-alcoholic fatty liver disease and its treatment with n-3 polyunsaturated fatty acids. *Clin Nutr*. 2018;**37**(1):37-55. [PubMed ID: 28139281]. <https://doi.org/10.1016/j.clnu.2017.01.006>.
37. Jump DB, Lytle KA, Depner CM, Tripathy S. Omega-3 polyunsaturated fatty acids as a treatment strategy for nonalcoholic fatty liver disease. *Pharmacol Ther*. 2018;**181**:108-25. [PubMed ID: 28723414]. [PubMed Central ID: PMC5743581]. <https://doi.org/10.1016/j.pharmthera.2017.07.007>.
38. Anania C, Perla FM, Olivero F, Pacifico L, Chiesa C. Mediterranean diet and nonalcoholic fatty liver disease. *World J Gastroenterol*. 2018;**24**(19):2083-94. [PubMed ID: 29785077]. [PubMed Central ID: PMC5960814]. <https://doi.org/10.3748/wjg.v24.i19.2083>.
39. Misciagna G, Del Pilar Diaz M, Caramia DV, Bonfiglio C, Franco I, Noviello MR, et al. Effect of a Low Glycemic Index Mediterranean Diet on Non-Alcoholic Fatty Liver Disease. A Randomized Controlled Clinical Trial. *J Nutr Health Aging*. 2017;**21**(4):404-12. [PubMed ID: 28346567]. <https://doi.org/10.1007/s12603-016-0809-8>.
40. Chiu S, Mulligan K, Schwarz JM. Dietary carbohydrates and fatty liver disease: de novo lipogenesis. *Curr Opin Clin Nutr Metab Care*. 2018;**21**(4):277-82. [PubMed ID: 29697539]. <https://doi.org/10.1097/MCO.0000000000000469>.
41. Yki-Jarvinen H, Luukkonen PK, Hodson L, Moore JB. Dietary carbohydrates and fats in nonalcoholic fatty liver disease. *Nat Rev Gastroenterol Hepatol*. 2021;**18**(11):770-86. [PubMed ID: 34257427]. <https://doi.org/10.1038/s41575-021-00472-y>.
42. Zhang S, Zhao J, Xie F, He H, Johnston LJ, Dai X, et al. Dietary fiber-derived short-chain fatty acids: A potential therapeutic target to alleviate obesity-related nonalcoholic fatty liver disease. *Obes Rev*. 2021;**22**(11). e13316. [PubMed ID: 34279051]. <https://doi.org/10.1111/obr.13316>.
43. Jensen T, Abdelmalek MF, Sullivan S, Nadeau KJ, Green M, Roncal C, et al. Fructose and sugar: A major mediator of non-alcoholic fatty liver disease. *J Hepatol*. 2018;**68**(5):1063-75. [PubMed ID: 29408694]. [PubMed Central ID: PMC5893377]. <https://doi.org/10.1016/j.jhep.2018.01.019>.
44. Zhang S, Li H, Meng G, Zhang Q, Liu L, Wu H, et al. Added sugar intake and its forms and sources in relation to risk of non-alcoholic fatty liver disease: results from the Tianjin Chronic Low-grade Systemic Inflammation and Health cohort study. *Br J Nutr*. 2022;1-8. [PubMed ID: 36156191]. <https://doi.org/10.1017/S000711452200277X>.
45. Kim MN, Lo CH, Corey KE, Luo X, Long L, Zhang X, et al. Red meat consumption, obesity, and the risk of nonalcoholic fatty liver disease among women: Evidence from mediation analysis. *Clin Nutr*. 2022;**41**(2):356-64. [PubMed ID: 34999330]. [PubMed Central ID: PMC8815093]. <https://doi.org/10.1016/j.clnu.2021.12.014>.